



# Exploring available options in characterising the health impact of industrially contaminated sites

Roberto Pasetto<sup>1,2</sup>, Piedad Martin-Olmedo<sup>3</sup>, Marco Martuzzi<sup>4</sup> and Ivano Iavarone<sup>1,2</sup>

<sup>1</sup>Dipartimento di Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Rome, Italy

<sup>2</sup>WHO Collaborating Centre for Environmental Health in Contaminated Sites, Istituto Superiore di Sanità, Rome, Italy

<sup>3</sup>Escuela Andaluza de Salud Publica, Granada, Spain

<sup>4</sup>European Centre for Environment and Health, World Health Organization, Bonn, Germany

## Abstract

Industrially contaminated sites (ICS) are of high concern from an environmental public health perspective, since industrial plants may produce a widespread contamination that can result in several health impacts on the populations living in their neighbourhood. The objective of this contribution is to briefly explore available options in studying the health impact of ICS, mainly referring to information provided by documents and activities developed by the WHO and the WHO Collaborating Center for Environmental Health in Contaminated Sites. In current practice the health impact of ICS is evaluated using studies and assessments falling in two broad types of strategies: one based on epidemiology and the other on risk assessment methods. In recent years, traditional approaches to assess relationships between environmental risks and health has been evolved considering the intricate nature between them and other factors. New developments should be explored in the context of ICS to find common strategies and tools to assess their impacts and to guide public health interventions.

## Key words

- contaminated sites
- health impact assessment
- epidemiology
- risk assessment
- industry
- chemical industry

## FOREWORD

WHO operationally defines contaminated sites (CS) as “Areas hosting or having hosted human activities which have produced or might produce environmental contamination of soil, surface or groundwater, air, food-chain, resulting or being able to result in human health impacts” [1]. Given this definition, an area affected by a single chemical contamination of a single environmental matrix (e.g., the soil contamination caused by a given pesticide), and a large area with soil, water, air, and food chain contamination by multiple chemicals (e.g., the contamination caused by long-term emissions of a petrochemical complex) can both be considered as a CS. Among CS, Industrially contaminated sites (ICS) are of high concern from an environmental public health perspective, since industrial plants may produce a widespread contamination that can result in several health impacts on the populations living in their neighbourhood. The assessment of the possible health impacts of ICS is challenging mainly due to the large extent of the affected contaminated areas, the coexistence of numerous toxic substances and the concurrence of several residential and/or occupational exposure pathways, with

highly variable time and space patterns. Associated health effects can be acute or chronic, severe or mild, specific or, more often, non-specific.

The methodology and practices in studying ICS and health are very heterogeneous, and this is not surprising given their complexity in environmental health and social issues. While some countries have acquired substantial experience in the field, many others have limited resources and less intensive research in ICS topics.

The international scientific debate on CS and health has been limited to few initiatives, like some international meetings organised by WHO [1].

In 2013, based on the activities carried out in the field of CS, the first WHO Collaborating Center on Environmental Health in Contaminated Sites was established at the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) ([http://www.euro.who.int/\\_\\_data/assets/pdf\\_file/0003/186240/e96843e.pdf?ua=1](http://www.euro.who.int/__data/assets/pdf_file/0003/186240/e96843e.pdf?ua=1)).

In 2015, on the basis of available evidence and experiences, and on expert consultations promoted by WHO, the COST Action “Industrially Contaminated Sites and Health Network” (ICSHNet) was launched

(COST Action IS1408: [http://www.cost.eu/COST\\_Actions/isch/Actions/IS1408](http://www.cost.eu/COST_Actions/isch/Actions/IS1408)). The ICSHNet Action aims at establishing and consolidating a European Network of experts and relevant institutions, and developing a common framework for research and response with the production of information for decision makers who have to deal with ICS issues.

The objective of this contribution is to briefly explore available options in studying the health impact of ICS, mainly referring to information provided by documents and activities developed by the WHO and the WHO Collaborating Center for environmental health in contaminated sites. Distinct research initiatives have provided significant pieces of evidence on how characterizing the health impact of ICS (see for example Mudu *et al.* 2014 [2]), but at present a clear-cut classification of approaches is not possible. In current practice the health impact of ICS is evaluated using studies and assessments falling in two broad types of strategies: one based on epidemiology and the other on risk assessment methods [1, 3]. Loosely speaking, these two strategies correspond to using health outcomes or environmental exposures, respectively, as a point of departure for an investigation.

## EPIDEMIOLOGICAL APPROACHES

Epidemiological studies conducted in ICS can be grouped in three main categories according to their aim:

1. description of the health profile of populations living in ICS, suggesting possible associations with local environmental risk factors;
2. analysis of the associations between environmental exposures and health outcomes and their causal nature, in order to test specific *a priori* hypotheses;
3. surveillance of the evolving pattern of the population health profile.

These three types of contributions are described in the following sections.

### Description of health profile

Some epidemiological methods can be adopted as a first basis for describing a population health profile. At a typical first level, such methods use routinely collected health data, broken down analysed at area or small area level. In these studies, each unit of study is identified as a population localized in a geographical area for which is possible to compute epidemiological indicators (*i.e.* both aggregated data on the population and on its health outcomes are available). These studies have the potential to be applied in several countries, given the relatively modest data requirements. They can be regarded as methods for a first-level approach because usually they do not require an *ad hoc* collection of data. Their main aim is to describe the health profile of populations, possibly generating hypotheses on local environmental risks.

There are several examples of such studies carried out in different sites using different outcomes as, for example, the one on hospital admissions near a large industrial area in France [4] or the cancer incidence study around a steel plant in the Netherlands, where

hierarchical Bayesian models were applied [5], both published in a monographic issue on ICS [3].

Typically, these studies require short time and low costs – though their interpretation is difficult. A notable example of a first level epidemiological approach is the one of SENTIERI implemented in Italy. The SENTIERI approach was developed to describe the health profile of populations living in national priority CS [6] by an *a priori* selection of health endpoints for which there exists evidence of association with the kind of industrial activities present in each site. In SENTIERI approach, the health outcomes are previously identified using the results of a review of the epidemiological literature on the health effects of the potential polluting activities occurring in CSs (named chemical industry, petrochemical plants and refineries, steel plants, power plants, mines and/or quarries, harbour areas, asbestos or other mineral fibres, landfills, and incinerators). The health profile of populations living in CSs is therefore firstly analysed evaluating the risks from the health outcomes characterized by an *a priori* interest. Health statistics are subsequently produced by using routinely collected data (for example, mortality and hospital discharge files and/or data from pathology registries, such as those on cancer and congenital malformations) and computing epidemiological indicators at area level. In SENTIERI approach, the selection of diseases on the basis of *a priori* evidence limits the typical biases of descriptive studies involving data dredging and multiple testing, which produce a lot of results and invite *post-hoc* interpretation.

General limitations of using “descriptive health profile approaches” are intrinsic to their “ecological epidemiological nature”. In these studies, health outcomes are estimated at group level rather than at the individual level and exposure to contaminants is attributed to each group using aggregate measures or qualitative indicators. Ecological associations can be difficult to interpret because of their aggregate nature; the exposure indicators do not reflect individual level exposure due to within-group heterogeneity in exposure and this is also the case for other factors which have a causative role for the health outcomes of interest. The more specific is the nature of the analysed associations and the homogeneity of within-group exposure, the more reliable can be the inferences on results. In every case, results from such approaches should be considered qualitatively and as clues to be deepened with other studies.

The usefulness of first level descriptive approaches in ICS depends also on the availability of data at an aggregate level such as to allow to distinguish communities living in the immediate neighborhood of ICS and experimenting all the complex milieu of exposures from the industrial plants, from populations which do no experiment such influences.

### Analysis of associations

Analytical epidemiological studies are based on study designs capable to examine hypothesized causal relationships and to make causal inferences. In general terms, analytical studies use individual data both on exposure and on health outcomes. However, in envi-

ronmental epidemiology and even more in epidemiological studies in ICS, the observational context limits data availability and collection. The common scenario is that environmental exposures are available at group level and mixed study design, with individual data on health outcome and aggregate data on exposure and on other predictive factors, are applied to test specific hypotheses.

When deciding for a given analytical epidemiological study in a ICS, several possible aspects of both the contamination and the exposed population must be considered, including: the presence of multiple sources of contamination; mixtures of contaminants; the evolution over time of contamination; the co-existence of different exposure pathways: soil, water, air, food-chain can be contaminated; the exposure routes and timing of exposure; the health outcomes of interests (and their characteristics in terms of etiology); the size of the population and of the exposed groups; the socioeconomic gradients and environmental justice issues; the co-existence of environmental and occupational exposures; the local demand and expectations.

An aspect of great importance in defining the study objectives is the time dimension – in particular, the latency time between exposure and different adverse health effects. In evaluating long-term effects, which typically characterize the health impact of long lasting contaminations, study designs capable of evaluating spatial differences, as ecological studies (especially at small-area level), cross-sectional studies (*e.g.*, biomonitoring), cohort and case-control studies are more suitable. For short-term effects, which are not common in ICS scenarios, study designs capable of evaluating temporal differences, as time series or case-crossover studies, and panel studies can be adopted.

The C8 Health Project, that examined the health consequences of a perfluorooctanoic acid (PFOA) release in air and in water bodies from a chemical plant, is a notable example of an approach that combines multiple study designs to verify hypotheses of local interest, and also achieve results of general validity ([www.c8sciencepanel.org/publications.html](http://www.c8sciencepanel.org/publications.html)) [7]. A panel of experts was established to evaluate if there was a “probable link” between PFOA exposure and any human disease. A Report was prepared for each selected health outcome, including a summary of the evidence for an association with exposure to PFOA.

In the C8 Health Project, a series of complementary studies were designed and carried out. They encompass assessments of environmental contamination and population exposures, including biomonitoring. A large range of epidemiological studies on the risk of *a priori* selected health outcomes (mortality, morbidity and cancer incidence and prevalence; birth outcomes, immune, hematopoietic, liver, kidney and endocrine function) were analysed in the general population, as well as in vulnerable subgroups, like children, and among workers employed in the polluting plant.

Information obtained carrying out such studies were useful both locally in defining priorities of interventions, and for general purposes in evaluating the health risk due to a given agent (PFOA). Even if the C8 Health

Project is a very interesting reference case-study, it is also an exception because of the specificity of the contamination (only one target chemical), while usually in ICS the contamination is from multiple chemicals. Also, economic resources are not often available to deploy a complete suite of studies.

In studying environment and health associations in ICS, it can be useful to integrate epidemiological geographical or micro-geographical studies (small-area) which use data at the population aggregated level, with typical analytical studies which use data at the individual level; an exemplary case of applying such approach is the one of the Taranto industrial area, a wide industrialized area with a long lasting contamination from different industrial plants, located close to an urban area [8].

An example of methods to verify associations between exposures from a given contamination source and health effects supposed to be associated to those exposures is the one called “funnel approach” [9]. This method progressively allows insights into the association between exposure and health effects through different phases, gradually shifting the evaluation from the population, small-area level, to the individual level. The approach is also based on a progressive refining of exposure assessment. It starts with a small-area analysis at the population level and ends with the individual human biomonitoring. It has been applied to verify the potential association between exposure to dioxin and the risk of non-Hodgkin’s lymphomas in areas affected by waste incinerators [9]. This approach is suitable when the source of contamination is well defined and specific, and the distribution of given pollutants can be estimated.

### Surveillance

Epidemiological surveillance in the environmental health field can be defined as “the systematic and continuous collection, analysis, interpretation of results, and dissemination of information on health profiles of populations associated with environmental factors for the planning, implementation and evaluation of risk management interventions” (modified from Tacker *et al.* 1996 [10]). In the context of areas contaminated by industrial activities, the epidemiological surveillance can be useful, for example, to evaluate the effectiveness of a remedial intervention or the reduction of the contamination and/or exposure, by analyzing the evolution of specific indicators over time.

To reach this aim the following methods can be applied: 1) a descriptive approach based on routinely collected data at area or small-area level; 2) analytical longitudinal studies such residential cohort studies; 3) cross sectional studies, as the one based on biomonitoring, with repeated surveys along time.

The descriptive approach can be based on defining outcomes of *a priori* interest depending on the contamination and the likely associated health effects; an example of such is the SENTIERI approach described above [6]. Cohort analytical epidemiological studies are generally applied for assessing a range of health outcomes in a population that was *a priori* identified according to suitable admissibility criteria. In the context

of ICS cohort studies are based on the recruitment of the population living in the contaminated area and followed up in time for outcomes with known or suspected links with the contamination [11, 12]. Therefore, with cohort studies, target populations can be monitored over time for their health status so helping in verifying the evolution of risks, for example as a consequence of remediation activities or public health interventions. Finally, cross sectional studies with repeated surveys over time can give the idea of the over time evolution of population exposure profiles or prevalence of health risk. Among cross-sectional studies, those of human biomonitoring have, for some pollutants (as for example, lead), the potential of evaluating the internal dose of contaminants so integrating the contribution of different pathways and routes of exposure [13].

### HUMAN HEALTH RISK ASSESSMENT APPROACHES AND TOOLS

Risk assessments carried out in CS are often based on a traditional risk assessment approach, *i.e.*, a multi-step procedure that leads to estimating the probability of the occurrence of disease as a function of exposure to one or more agents. It often includes a comparison of estimated potential exposure to a reference value – for example, a comparison between measured exposure levels and a tolerable dose established by toxicology.

In some countries the institutions responsible for risk assessment of ICS are well identified and use standardised procedures and tools. For example, in the US, the Environmental Protection Agency (EPA) has developed a specific set of tools for risk assessment in ICSs, implemented in the frame of the US Federal Government's program to clean up the nation's uncontrolled hazardous waste sites, called Superfund. Each Superfund site is unique in terms of the present contaminants and their potential health effects. Therefore, EPA conducts risk assessments on a site-by-site basis. The risk assessment estimates the current and possible future risks if no remediation action is undertaken ([http://www.epa.gov/oswer/riskassessment/risk\\_superfund.htm](http://www.epa.gov/oswer/riskassessment/risk_superfund.htm)). Among the procedures applied by public institutions in evaluating the health impact of ICS, special mention should be given to the Public Health Assessment (PHA), an approach developed by the US Agency for Toxic Substances and Disease Registry (ATSDR). ATSDR has been required by law to conduct public health assessments at each of the sites on the EPA National Priorities List. The aim of these evaluations is to establish if people are being exposed to hazardous substances and, if so, whether that exposure is harmful and should be stopped or reduced. ATSDR considers the same environmental data as the EPA, but focuses more closely on site-specific exposure conditions, specific community health concerns, and any available health outcome data to provide a more comprehensive and qualitative evaluation of possible public health hazards. The PHA procedure is designed to reach its objectives by combining health risk assessment procedures with an epidemiological descriptive assessment ([www.atsdr.cdc.gov/hac/PHAManual/toc.html](http://www.atsdr.cdc.gov/hac/PHAManual/toc.html)). In fact, PHA combines quantitative risk assessment procedures with

an approach that also evaluates health outcome data, when available, to identify whether rates of disease or death are elevated in a site community, especially if the community expresses concern about a particular outcome (*e.g.*, cancer).

Many tools are available for risk assessment in CS on a single pollutant basis; they are sophisticated, well-founded, mainly focused on specific exposure pathways associated with soil contamination or air pollution [1], and providing a series of defaults values and statistics as, for example, the European Exposure Factors (ExpoFacts, <http://expofacts.jrc.ec.europa.eu/>).

Over the years, many risk assessments in CS have focused on the measurement of the health impacts due to chemicals, individually, and through individual pathways. However, in the last years the science of risk assessment has developed and has paid attention to the need to explore the intricate relationship between risk factors. In fact, the causal pathway leading to an adverse health outcome does not necessarily result from the independent contribution of concurrent risks, but can involve interactions between agents such as chemicals with other conditions, for example those related to the socioeconomic and cultural contexts in which environmental risks take place [14-16]. New developments and frontiers in risk assessment consider the intricate relationships within environmental risks and between them and other factors; relationships which typically characterize the contexts of ICS. Examples of such developments are the multipollutant approach and the incorporation of nonchemical stressors in community-based risk assessment [17, 18].

The multipollutant approach deals with the evaluation of both the health effects of pollutant mixtures, as well as the effects of single pollutants in a multipollutant context as those typical of complex contaminated areas. Characterizing exposure to multipollutant mixtures requires an advanced understanding of the sources of pollutants, the chemical transformations and interactions between multiple pollutants, and information on the correlations in space and time between their individual concentrations. The most relevant consideration for risk assessment in a multipollutant context is how different mixtures contribute to the overall exposures of populations and to distinguish which mixtures or parts of mixtures are most closely associated with particular health outcomes [17].

Another important recent development is the community-based risk assessment, *i.e.*, the examination of all stresses affecting a defined population or community, including both the complex milieu of chemicals to which the community is exposed and its specific vulnerabilities which depends, among the others, on the composition of the population in terms of vulnerable subgroups (*e.g.*, children), the socioeconomic conditions, the prevalence of personal habits which contribute to risk (*e.g.*, smoking). Non-chemical stressors make up an important subset of community vulnerabilities that have the potential to either directly affect the health of individuals or modulate their response to chemical exposures. Strides have been made in developing methods for conducting a cumulative risk assessment for multiple chemicals, but



integrating non-chemical stressors – physical or psychological – represents a new challenge. Furthermore, the inclusion of nonchemical stressors in cumulative risk assessments may enable risk assessors to identify those segments of the population who are more susceptible or vulnerable to the effects of chemical stressors [18].

Recently, important research efforts have been invested considering the complexity of environmental risk factor scenarios. In Europe the research projects INTARESE ([www.intarese.org](http://www.intarese.org)) and HEIMTSA ([http://www.innovationseeds.eu/Virtual\\_Library/Results/HEIMTSA.kl](http://www.innovationseeds.eu/Virtual_Library/Results/HEIMTSA.kl)) were set up integrating epidemiological models that provide an overall qualitative/quantitative assessment of the impact on health of environmental stressors by taking into account multiple risk factors, combined exposure pathways and cumulative health outcomes. Notwithstanding these developments, the question of how to apportion causality between two or more interacting factors remains unsolved [15]. In US the EPA developed the NexGen project to design the next generation of risk science. The NexGen approach gives strong emphasis on problem formulation to ensure that risk assessments are designed in a way that can support decision makers. It is based on three phases [19]: after establishing the risk science objectives in phase I, a scientific assessment of risk using the best available scientific tools and technologies is undertaken in phase II. Phase III involves the use of scientific evidence in risk management decision-making context, taking into account extra-scientific considerations such as economic analysis, sociopolitical considerations, and public perception of risk [19]. Regarding risk assessment, the NexGen framework expands the classical Red Book four step evaluation [20] to incorporate a population health approach, new directions in toxicity testing, and new risk assessment methodologies. All determinants of health and their combination are considered dividing them in three categories: biological and genetic, environmental and occupational, and social and behavioral. Environmental determinants include contaminants in air, food, water, or soil, as well as the built environment, so considering the wide spectrum and complexity which is typically present in ICS.

Both the recent innovative developments in EU and US promote decision guided and holistic approaches to risk science which seem to be very suitable to be specifically implemented for risk assessments in the complex scenarios of ICS.

A potentially promising tool to be applied to ICS, involving integrated measures of population health, is represented by the of Environmental Burden of Disease (EBD) approach. The use of such methodology as comparative risk assessment is based on producing or (more frequently) gathering and compiling epidemiological evidence and dose-response functions and estimating the excess health risk associated with different exposure scenarios. Quantifications of EBD could therefore be a useful instrument for setting priorities in environmental health policies and research in ICS. A recent example of the use environmental burden of disease is the overall assessment of the health impact of nine environmental risk factors in six European countries (benzene, dioxins,

secondhand smoke, formaldehyde, lead, traffic noise, ozone, particulate matter (PM<sub>2.5</sub>), and radon [21]).

## DISCUSSION

Industrially contaminated sites are of high concern from an environmental public health perspective at local, regional and global scale. In Europe, industrial activities, including industrial waste disposal and treatment, cause the majority of the overall contamination ([http://eussoils.jrc.ec.europa.eu/ESDB\\_Archive/eussoils\\_docs/other/EUR26376EN.pdf](http://eussoils.jrc.ec.europa.eu/ESDB_Archive/eussoils_docs/other/EUR26376EN.pdf)).

Several other aspects contribute to make ICS and health a relevant public health issue: industrial contaminations usually affect different environmental media and concern complex mixtures of chemicals of toxicological importance; social, occupational, environmental and health issues are strongly interconnected in these areas. Disadvantaged people are found to live in many polluted areas, near industrial and waste dumping sites, with poor-quality housing and limited access to green space and to good quality health services [22, 23].

Health impact assessments in ICSs do exist, yet the overall impact of ICSs is still unknown, due to fragmentation of objectives and methods, the lack of integrated evaluating approaches, and the large variety of contaminated areas.

Several different approaches and tools are currently available. However, since most of them have been developed in specific contexts (urban areas), or to address specific problems (e.g., air pollution, wastes, food chains), and given the high heterogeneity in type of ICS and in the data and resources availability, there is a need to identify appropriate tools and methodologies able to account for the complex mix of environmental, health and social issues in ICSs. It is therefore urgent to move forward using suitable and harmonized strategies. The ecosystems-enriched Drivers, Pressures, State, Exposure, Effects, Actions or 'eDPSEEA' model, proposed by Reis et al [24], is a good example of a framework in which developing integrated approaches. Such model is driven by sustainable development goals. It is focused on promoting both the human health and well-being (with emphasis on vulnerable population subgroups, like children, pregnant women, elderly people, ethnic minorities, and workers), while safeguarding ecosystems.

A promising tool possibly suitable for ICS is exemplified by the Integrated Environmental and Health Impact Assessment (IEHIA), a multidisciplinary instrument that draws from many different disciplines, like public health, social and political sciences, environmental science, urban planning, epidemiology and statistics [15]. The possibility to estimate the EBD associated with living in ICSs, possibly accounting for socioeconomic factors, is another promising tool, valuable also to compare the impact of different pollutants on diverse health outcomes, in heterogeneous industrial polluted areas.

The COST Action IS1408 has established a network of 30 countries, involving about 100 researchers and experts in environmental health topics related to ICS. The Action is expected to contribute to providing participat-

ing countries with proper tools and harmonised methodologies in characterising the health impacts of ICSs, by a) clarifying knowledge gaps and research priorities; b) supporting collection of relevant data and information; c) stimulating development of harmonised methodology; d) promoting collaborative research initiatives, and developing guidance and resources on risk and impact assessment, management and communication, training and mobility of young research across Europe.

Interactions between the COST Action ICSHNet and the European Environment and Health Process lead by WHO are well developed. The Roadmap to the sixth Conference of European Ministries in the sectors of Health and Environment, identifies 8 major environmental health themes: air, water, energy, chemicals, food, cities, climate change and disasters, and waste. The ICSHNet is likely to deal with several of these themes, for example by identifying the most informative assessments with reference to the best available policy options, creating the conditions for undertaking

comparable Health Impact Assessments of ICSs, and helping to transfer scientific evidence into the policy making process.

Environmental health and social issues related to industrial contamination, including industrial wastes, must be addressed through an intersectoral approach if we want to protect the environment and the public health and maximise wellbeing and prosperity in such areas. Therefore, the strategies to assess the health dimension of living in ICS have to be seen as part of a social negotiation, where the legitimate needs and aspirations of residents, vulnerable groups, workers, and investors are taken into account, in a fair process.

### Conflict of interest statement

The authors declare that they have no conflicts of interest.

Submitted on invitation.

Accepted on 29 January 2016.

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